DOCKET NO.: ISPH-0794 (ISIS0171-100) **PATENT**

In the Claims:

The current status of all claims is listed below and supercedes all previous lists of claims.

1-16. (*cancelled*).

17. (*currently amended*) A method of selecting an effective antisense oligonucleotide sequence for inhibition of expression of a preselected target nucleic acid comprising:

providing a set of antisense oligonucleotide sequences ~~of a selected~~ 12 to 25 nucleotides in length which are complementary to a preselected target nucleic acid sequence;

selecting an antisense oligonucleotide sequence from a set of antisense oligonucleotide sequences, wherein the selected antisense oligonucleotide sequence comprises at least one activity-enhancing oligonucleotide sequence motif selected from 5'-CCAC-3', 5'-CCA-3', 5'-TCCC-3', 5'-CCCA-3', 5'-CCCT-3', 5'-CCCC-3', 5'-ACTC-3', 5'-ATCC-3', 5'-CACC-3', 5'-GCCA-3', 5'-ATC-3', 5'-CAC-3', 5'-CTC-3', 5'-GCAT-3', 5'-ACCA-3', 5'-CATC-3', 5'-TCC-3', 5'-AAC-3', or 5'-CTCT-3'; and

no activity-decreasing sequence motifs selected from 5'-GGGG-3', 5'-GGG-3', 5'-GGCT-3', 5'-TAAA-3', 5'-ACTG-3', 5'-GAAA-3', 5'-TGGG-3', 5'-AAAT-3', 5'-GGA-3', 5'-CTGG-3', 5'-ATAA-3', 5'-AATA-3', 5'-CCGG-3', 5'-ATA-3', 5'-GGAG-3', 5'-CTG-3', 5'-AAA-3' or 5'-AAA-3'.

~~and wherein the set of antisense oligonucleotide sequences are of a selected length which are complementary to a preselected target nucleic acid sequence~~.

Claims 18 - 31 (*cancelled*)

32. (*New*) An antisense oligonucleotide produced by the method of claim 17.

33. (*New*) An antisense oligonucleotide of claim 32, wherein said antisense oligonucleotide is chimeric.

34. (*New*) An antisense oligonucleotide of claim 34, wherein said oligonucleotide comprises a 2'-methoxyethyl nucleoside modification.

35. (*New*) An antisense oligonucleotide 12 to 25 nucleotides in length targeted to a preselected target RNA, comprising:

at least one 2'modified nucleoside; and

at least two activity-enhancing sequence motifs selected from 5'-CCAC-3', 5'-CCA-3', 5'-TCCC-3', 5'-CCCA-3', 5'-CCCT-3', 5'-CCCC-3', 5'-ACTC-3', 5'-ATCC-3', 5'-CACC-3', 5'-GCCA-3', 5'-ATC-3', 5'-CAC-3', 5'-CTC-3', 5'-GCAT-3', 5'-ACCA-3', 5'-CATC-3', 5'-TCC-3', 5'-AAC-3', or 5'-CTCT-3'.

36. (*New*) An antisense oligonucleotide of claim 35, further having no activity-decreasing sequence motifs selected from 5'-GGGG-3', 5'-GGG-3', 5'-GGCT-3', 5'-TAAA-3', 5'-ACTG-3', 5'-GAAA-3', 5'-TGGG-3', 5'-AAAT-3', 5'-GGA-3', 5'-CTGG-3', 5'-ATAA-3', 5'-AATA-3', 5'-CCGG-3', 5'-ATA-3', 5'-GGAG-3', 5'-CTG-3', or 5'-AAA-3'.

37. (*New*) An antisense oligonucleotide of claim 35, wherein said antisense oligonucleotide is chimeric.

38. (*New*) An antisense oligonucleotide of claim 35, wherein said oligonucleotide comprises a 2'-methoxyethyl nucleoside modification.